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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 08/653,294 | 05/24/1996 | CAROL CLAYBERGER | 286002020023 | 5995 |

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| EXAMINER | |
|---|---|
| DIBRINO, MARIANNE NMN | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

DATE MAILED: 12/03/2003

65

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 08/653,294 | CLAYBERGER ET AL. | |
| | Examiner | Art Unit | |
| | DiBrino Marianne | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**P riod for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 September 2003 and 02 June 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2-4,12,13,15-21 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *15 and 17* is/are allowed.

6)☒ Claim(s) *2-4,12,13,18-21 and 27* is/are rejected.

7)☐ Claim(s) *16* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

1. In view of the appeal brief filed on 9/2/03, PROSECUTION IS HEREBY REOPENED. A new ground of rejection is hereby set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:
(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,
(2) request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131 or 1.132) or other evidence are permitted. See 37 CFR 1.193(b)(2).

2. Applicant's amendment filed 6/2/03 (Paper No. 59 is acknowledged and has been entered.

3. Claims 2-4, 12, 13 and 15-21 and 27 are pending.

Claims 2-4, 12, 13, 15-21 and 27 are presently being examined.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 2-4, 12, 13, 18-21 and 27 are rejected under 103(a) as being unpatentable over WO 88/05784 in view of Wong et al (Human Immunology 1992, 35/3, 200-208), U.S. Patent No. 5,073,540 and U.S. Patent No. 5,478,925.

WO 88/05784 teaches peptides which are cross reactive with portions of the $\alpha 1$ or $\alpha$ 2 domains of MHC class I, with the sequence of those of the instant claims (especially claim 1 and abstract). WO 88/05784 also teaches modification of such peptides using conventional techniques to extend their biological half lives (especially pages 21-23). Page 10 of the instant application discloses such conventional techniques. WO 88/05784 explicitly teaches use of such peptides for prolonging graft survival time by reducing rejection caused by CTL. WO 88/05784 teaches using the said peptides linked to other peptides or proteins of interest when

WO 88/05784 does not teach dimerization of the peptides.

Wong et al teaches foci of TCR receptor aggregation upon binding to MHC class I molecules.

Patent No. 5,073,540 discloses peptides useful as antagonists or agonists for membrane receptors, one portion comprising the same structure as the peptides of the instant application (especially columns 7 and 8). Patent No. 5,073,540 further discloses that oligopeptides may be employed that are capable of mimicking the site of the Class I antigen associated with binding to the receptor, thus substituting for the class I antigen (especially paragraph spanning columns 4 and 5).

U.S. Patent No. 5,478,925 discloses receptors that exist in aggregated form when exposed to ligand. U.S. Patent No. 5,478,925 further discloses binding proteins that are identical to the extra-cellular domains of the said receptors that compete for binding and that the monomers must be administered in very high doses in order to result in effective inhibition of binding when administered to humans. U.S. Patent No. 5,478,925 discloses that multimers of the proteins are more effective in inhibiting activity at lower doses, since they can effectively compete for binding sites on the aggregates of the cell surface receptors. (especially columns 1, 2 and 3).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the prior art peptides taught by WO 88/05784 as multimers, i.e., at least dimers, as is taught by U.S. Patent No. 5,478,925 for other receptor mimicking and inhibiting polypeptides, and to test functional activity on surface receptors or lymphocyte activity of the modified peptides using the assays taught by WO 88/05784 (especially page 25), and to use the said multimeric peptides in the method of inhibiting graft rejection taught by WO 88/05784 for prolonging graft survival time by reducing rejection caused by CTL which comprise TCR that aggregate upon binding to MHC class I molecules as taught by Wong et al.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to stimulate or inhibit membrane receptors as taught by WO 88/05784 and as disclosed by Patent No. 5,073,540 and/or to prolong graft survival time as taught by WO 88/05784 because Wong et al teaches that TCR on CTL aggregate upon binding class I MHC and U.S. Patent No. 5,478,925 discloses that multimers are more effective in inhibiting activity at lower doses since they can effectively compete for binding sites on the aggregates of cell surface receptors and because one of ordinary skill in the art at the time the invention was made would have expected the dimmers of the same unit to exert the same functional effects as a monomer.

6. Claims 2-4, 12, 13, 18-21 and 27 are rejected under 103(a) as being unpatentable over WO 88/05784 in view of U.S. Patent No. 6,419,931.

WO 88/05784 teaches peptides which are cross reactive with portions of the α1 or α 2 domains of MHC class I, with the sequence of those of the instant claims (especially claim 1 and abstract). WO 88/05784 also teaches modification of such peptides using conventional techniques to extend their biological half lives (especially pages 21-23). Page 10 of the instant application discloses such conventional techniques. WO 88/05784 explicitly teaches use of such peptides for prolonging graft survival time by reducing rejection caused by CTL. WO 88/05784 teaches using the said peptides linked to other peptides or proteins of interest when

WO 88/05784 does not teach dimerization of the peptides.

U.S. Patent No. 6,419,931 discloses that peptides that modulate CTL can be combined to form multimers and that the same peptide can be linked to itself to form a homopolymer, i.e., a dimer (especially column 17 at lines 4-38-43).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the prior art peptides taught by WO 88/05784 as dimers as disclosed by taught by U.S. Patent No. 6,419,931, and to test functional activity on surface receptors or lymphocyte activity of the modified peptides using the assays taught by WO 88/05784 (especially page 25), and to use the said multimeric peptides in the method of inhibiting graft rejection taught by WO 88/05784 for prolonging graft survival time.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to stimulate or inhibit membrane receptors as taught by WO 88/05784 and to prolong graft survival time as taught by WO 88/05784 because U.S. Patent No. 6,419,931 discloses that peptides that modulate CTL can be combined to form multimers and that the same peptide can be linked to itself to form a homopolymer, i.e., a dimmer, and one of ordinary skill in the art at the time the invention was made would have expected the dimmers of the same unit to exert the same functional effects as a monomer.

7. Claim 16 is objected to for depending upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

8. Claims 15 and 17 are allowable.

9. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 703-308-0061 (after 1/7/04 the telephone number is 571-272-0842). The Examiner can normally be reached on Monday and Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Chan, can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306 (before final) or 703-872-9307 (after final).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
November 28, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600